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August 5, 2005



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Center Food Safety and Applied Nutrition
Food and Drug Administration (HFS-830)
5100 Paint Branch Parkway
College Park, MD 20740-3835 Via certified mail with return slip #7003 2260 0007 5983 9654

RE: Qualified Health Claim Petition: Green Tea and Reduced Risk of Cancer (Docket No. 2004-0083)-
Request for Reconsideration in accordance with 21 C.F.R. 10.33

Dear Dr. Schneeman:

Thank you for your letter dated July 28, 2005. Per your suggestion, please accept this document and my previous letters dated July 1, July 5 (including its attached references) and July 6, 2005 to Mr. Michael M. Landa as a formal request for administrative reconsideration of the FDA June 30, 2005 action on the above referenced petition.

## A. Decision involved

The undersigned respectfully requests that the FDA reconsider the conclusions which were published on June 30, 2005 as the result of the review of my application which was submitted to the FDA on January 17, 2004 under Docket No. 2004Q-0083. The FDA conclusions read:

***"Two studies do not show that drinking green tea reduces the risk of breast cancer in women, but one weaker, more limited study suggests that drinking green tea may reduce the risk. Based on these studies, FDA concludes that it is highly unlikely that green tea reduces the risk of breast cancer"***

***"One weak and limited study does not show that drinking green tea reduces the risk of prostate cancer, but another weak and limited study suggests that drinking green tea may reduce the risk. Based on these studies, FDA concludes that it is highly unlikely that green tea reduces the risk of prostate cancer"***

## B. Action requested

Based on the scientific evidence that the FDA relied on for its decision, the undersigned respectfully requests that the FDA modify the language of its conclusions to read as follows:

"Drinking green tea equivalent to that consumed by Asian Americans may reduce the risk of breast cancer in women. There is credible evidence supporting this claim although the evidence is limited."

"Drinking green tea equivalent to that consumed by the residents living in Hangzhou, China may reduce the risk of prostate cancer. There is credible evidence supporting this claim although the evidence is limited."

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## C. Statement of grounds

The June 30, 2005 FDA conclusions need to be modified for the following reasons:

I. The conclusions contain confusing language. For examples, the Foxnews reported that the FDA rejects the green tea claim (1). The American Herbal Products Association said that the FDA allows the qualified health claim (2). The Reuters avoided interpretation and simply stated that the FDA has made a conclusion "contrary to what some studies claim" (3). The opinions expressed by the semi-informed consumers are amusing, but damaging to the FDA credibility as a respectable federal agency (4). The nutraingredients industry dismisses the FDA statement as irrelevant (5). The ordinary consumers are totally confused by these news. Therefore, the FDA should clarify the language of its conclusions so that it can be understood by people other than lawyers specialized in the food and diet labeling law.

II. The FDA had relied on two articles to reach its conclusions that green tea does not reduce the risk of breast cancer and prostate cancer. The first of these two articles authored by Suzuki Y, Tsubono Y, Nakaya N, Suzuki Y, Koizumi Y, Tsuji I, entitled "Green tea and the risk of breast cancer: pooled analysis of two prospective studies in Japan", is a Short Communication in British Journal of Cancer 2004;90:1361-1363 first published online 24 February, 2004 (6). The second of these two articles authored by Sonoda T, Nagata Y, Mori M, Miyanaga N, Takashima N, Okumura K, Goto K, Naito S, Fujimoto K, Hirao Y, Takahashi A, Tsukamoto T, Fujioka T, Akaza H and entitled "A case-control study of diet and prostate cancer in Japan: possible protective effect of traditional Japanese diet" was published in Cancer Science 2004 (March);95:238-242 (7). Both of these two articles were published after January 17, 2004, the official date of my submission. Based on your letter of July 28, 2005, you indicate that any information not included in my original petition will not be considered in my seeking reconsideration of the 2004Q-0083 petition. As a result of your ruling, the Suzuki et al. (6) and the Sonoda et al. (7) reports, should not have been used by the FDA in weighing the scientific evidence for its green tea decision in the first place because they were made public after January 17, 2004, the date of my submission.

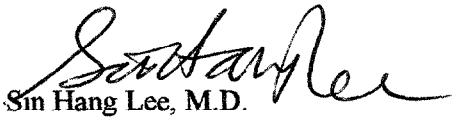
III. Even if the Suzuki et al.'s and the Sonoda et al.'s reports were to be considered, they should have been rejected for lack of scientific merits. The Suzuki et al.'s Short Communication (6) pooled the numbers of breast cancer patients from two previous series, one originally designed for gastric cancer statistics by Tsubono Y, Nishino Y, Komatsu S et al. [Green tea and the risk of gastric cancer in Japan. N Engl J Med 2001;344:632-636] (8) and the other for personality/cancer study by Nakaya N, Tsubono Y, Hosokawa T et al. [Personality and the risk of cancer. J NCI 2003; 95:799-805] (9), respectively. Although the Suzuki et al.'s Short Communication claims to consist of two cohort studies, the data were collected by a single department under the direction of the same principal investigator, Y Tsubono (Correspondence author is identified as Y Tsubono in all three references 6, 8 and 9), by self-administered questionnaires returned by the survey subjects living in Miyagi prefecture in rural northern Japan. As I pointed out in my July 5, 2005 letter to Mr. Landa, the biggest flaw in these two studies under the direction of Tsubono is that "...**in Japan at the time of the survey, the majority of patients with cancer were not told the true diagnosis**..." and that "..**the diagnosis of adenocarcinoma had been histologically confirmed in 80 percent of the cases**."(8) In other words, 20 percent of the so-called cancer patients in all Tsubono's data collected in Miyagi might not have cancer at all. The statistical error might have been further augmented by those patients who might have cancer, but did not report as having cancer in their returned questionnaires because they were not told the true diagnosis. It is questionable if Mr. Landa had even read the Nakaya et al.'s study originally designed for personality/cancer research (9). If he had, he would have discovered the discrepancy between the number of breast cancer patients listed in the Nakaya et al.'s original report and that listed in the Suzuki et al.'s Short Communication. The Nakaya et al.'s report is not listed as a reference in the FDA letter of enforcement dated June 30, 2005.

IV. As I pointed out in my July 5, 2005 letter to Mr. Landa, the residents living in rural northern Japan, for example, in Miyagi and in Hokkaido, generally do not have easy access to quality green tea like those living around tea plantation regions of the middle south of the nation. To select two series of green tea

studies conducted in northern Japan as the weighing evidence for making a negative general statement on behalf of the FDA will not be accepted by the world's scientific community nor by the educated American consumers. It does not need a statistician to explain why the 95% CIs do not show a significant *p* for trend for an inverse relationship between green tea consumption and prostate cancer incidence in the Sonoda et al.'s article (7). The analogy is to perform a statistical study by conducting self-administered questionnaire surveys among the Eskimos living in Alaska to study the effectiveness of eating orange fruits in reducing human cancer risk, and to mix the data collected from Alaska with those collected from the residents living in the Indian River county of the state of Florida as one homogenous mass to determine if orange fruits are beneficial in reducing cancer risk. It would be dangerous to draw any scientific conclusion from such analyses. It is simply common sense.

Thank you for your reconsideration and I will be glad to make myself available to meet with you and the FDA reviewers if necessary to facilitate this reconsideration process.

Sincerely,



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References (enclosed 1-5)

(1) July 6, 2005 Foxnews: FDA rejects green tea cancer claims.
(2) July 7, 2005 AHPA Update: FDA allows qualified health claims for green tea for reducing risk of breast and prostate cancer.
(3) July 1, 2005 Reuters: Green tea doesn't lower cancer risk, U.S. FDA says.
(4) July 1, 2005 ImmInst.org: Green tea unlikely to reduce cancer risk.
(5) 8/3/2005 Nutraingredients-USA: Green tea stirs growth, despite FDA anticancer doubts.
(6) Suzuki Y, Tsubono Y, Nakaya N, Suzuki Y, Koizumi Y and Tsuji I. Green tea and the risk of breast cancer: pooled analysis of two prospective studies in Japan. Short Communication in British Journal of Cancer 2004;90:1361-1363 (copy submitted on July 5, 2005. Published on line 2/24/04)
(7) Sonoda T, Nagata Y, Mori M, Miyanaga N, Takashima N, Okumura K, Goto K, Naito S, Fujimoto K, Hirao Y, Takahashi A, Tsukamoto T, Fujioka T, and Akaza H. A case-control study of diet and prostate cancer in Japan: possible protective effect of traditional Japanese diet. Cancer Science 2004 (March);95:238-242 (copy submitted on July 5, 2005)
(8) Tsubono Y, Nishino Y, Komatsu S, Hsieh CC, Kanemura S, Tsuji I, Nakatsuka H, Fukao A, Satoh H, Hisamichi S. Green tea and the risk of gastric cancer in Japan. N Engl J Med 2001;344:632-636 (copy submitted on January 17, 2004)
(9) Nakaya N, Tsubono Y, Nishino Y, Hosokawa T, Fukudo S, Shibuya D, Akizuki N, Yoshikawa E, Kobayakawa M, Fujimori M, Saito-Nakaya K, Uchitomi Y, and Tsuji I. Personality and the risk of cancer. J NCI 2003; 95:799-805 (copy submitted on July 5, 2005)